

plasma in humans or animals, characterized in that it has a slow release only of vitamin C and a plain release only of vitamin E; *written descr. ? 112(1) ? No.*

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wherein vitamin C is present in an amount in the delivery system so as to deliver a daily dose corresponding to 60 mg - 2 g of vitamin C, and vitamin E is present in an amount in the delivery system so as to deliver a daily dose corresponding to 50 mg - 500 mg of α -tocopherol;

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wherein the solubility of the vitamin E is such that at least 90% of the vitamin E is dissolved in less than 30 minutes under the conditions of Test B; and

wherein the solubility of the vitamin C is such that less than 40% of the vitamin C is dissolved after 1 hour under the conditions of Test A; and

wherein said delivery system achieves a concentration of vitamin E in the blood plasma of at least 20 $\mu\text{mol/liter}$ and a concentration of vitamin C in the blood plasma of at least 40 $\mu\text{mol/liter}$.

39. (New) A pharmaceutical delivery system according to claim 38, characterized in that it is a system comprising a tablet comprising at least two non-identical delivery principals, wherein

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- a) one delivery principal comprises
 - i) vitamin C;
 - ii) a pharmaceutically acceptable excipient for controlling the slow release of vitamin C; and
 - iii) optionally, at least one other pharmaceutically acceptable excipient; and
 - b) another delivery principal comprises

Sub B
Contd

- i) vitamin E; and
- ii) at least one pharmaceutically acceptable excipient.

40. (New) A pharmaceutical delivery system according to claim 38, characterized in that the antioxidants are present in amounts so as to obtain vitamin C and vitamin E in a ratio in the blood plasma of 1:1 to 3:1.

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41. (New) A pharmaceutical delivery system according to claim 40, characterized in that the system achieves a ratio between vitamin C and vitamin E in the blood plasma that is about 2.2:1.

42. (New) A pharmaceutical delivery system according to claim 38, characterized in that the antioxidants are present in amounts so as to raise the concentration of vitamin E in human blood plasma to at least 30 $\mu\text{mol/liter}$.

43. (New) A pharmaceutical delivery system according to claim 38, wherein the antioxidants are present in amounts so as to raise the concentration of vitamin E in human blood plasma to at least 50 $\mu\text{mol/liter}$.

44. (New) A pharmaceutical delivery system according to claim 38, wherein the antioxidants are present in amounts so as to raise the concentration of vitamin C in blood plasma to at least 60 $\mu\text{mol/liter}$.

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45. (New) A pharmaceutical delivery system according to claim 38, wherein the antioxidants are present in amounts so as to raise the concentration of vitamin C in blood plasma to at least 100 $\mu\text{mol/liter}$.

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Part B

46. (New) A pharmaceutical delivery system according to claim 38, characterized in that vitamin C is ascorbic acid and vitamin E is selected from the group consisting of d- α -tocopheryl acetate, d- α -tocopheryl acid succinate, d- α -tocopherol, d- β -tocopherol, d- γ -tocopherol, d- δ -tocopherol, d- α -tocotrienol, d- β -tocotrienol, d- γ -tocotrienol, d- δ -tocotrienol, dl- α -tocopherol, dl- α -tocopheryl acetate, dl- α -tocopheryl calcium succinate, dl- α -tocopheryl nicotinate, dl- α -tocopheryl linoleate/oleate, and all other possible derivatives or stereo isomeric forms of the above compounds.

47. (New) A pharmaceutical delivery system according to claim 38, wherein vitamin C is provided in an amount sufficient to deliver 100 mg - 1.5 g of ascorbic acid per day.

48. (New) A pharmaceutical delivery system according to claim 38, wherein vitamin E is provided in an amount sufficient to deliver 100 mg - 250 mg of α -tocopherol per day.

49. (New) A pharmaceutical delivery system according to claim 38, wherein the vitamin C and E is delivered by 1 to 8 dosage units per day.

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50. (New) A pharmaceutical delivery system according to claim 38, wherein the vitamin C and E are delivered by 1 or 2 dosage units per day.
51. (New) A pharmaceutical delivery system according to claim 50, wherein the daily dose of vitamin C and E is delivered by 2 dosage units, each dosage unit comprising i) from approximately 200 to 300 mg of vitamin C and ii) approximately 80 to 120 mg of vitamin E.
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52. (New) A pharmaceutical delivery system according to claim 38, characterized in that less than 40% of the vitamin C is dissolved after 1 hour under the conditions of Test A, from 50 to 80% of the vitamin C is dissolved after 3 hours under the conditions of Test A, and more than 90% of the vitamin C is dissolved after 7 hours under the conditions of Test A.
53. (New) A pharmaceutical delivery system according to claim 38, characterized in that at least 90% of the vitamin E is dissolved in less than 15 minutes under the conditions of Test B.
54. (New) A pharmaceutical delivery system according to claim 38 for treating conditions, diseases, and disorders involving oxidative stress.
55. (New) A pharmaceutical delivery system according to claim 54, wherein the conditions, diseases, and disorders involving oxidative stress are selected from the group consisting of atherosclerosis, cancer, type I diabetes, type II diabetes, diabetic nephropathy, skin

damage, scar tissue, central nervous system disorders and degeneration, neural degeneration, Alzheimer's Disease, inflammation, fertility/fecundity diseases and disorders, conditions, diseases, and disorders related to sun exposure, diseases and disorders related to aging, cataracts, inappropriate coagulation, and nitrate intolerance.

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56. (New) A pharmaceutical delivery system according to claim 55, wherein the conditions, diseases, and disorders involving oxidative stress are selected from the group consisting of atherosclerosis, type I diabetes, type II diabetes, diabetic nephropathy, central nervous system disorders and degeneration, neural degeneration, Alzheimer's Disease, conditions, diseases and disorders related to sun exposure, and cataracts.

composition
claim. no part. wt.
no 110, 1
Cvad(E)

57. (New) A method of treating oxidative stress disorders and associated diseases and conditions, said method comprising administering to an individual a combination of vitamin C and vitamin E in sufficient amounts to raise the concentration of said vitamins in blood plasma to a level sufficient to treat oxidative stress disorders, and to a ratio of approximately 1:1 to 3:1, in not more than 8 weeks from the first administration,

wherein the method achieves a concentration of vitamin E in the blood plasma that is at least 20 $\mu\text{mol/liter}$ and a concentration of vitamin C in the blood plasma that is at least 40 $\mu\text{mol/liter}$; and

wherein the administering is in amounts corresponding to a daily dose of 60 mg - 2 g of vitamin C and corresponding to a daily dose of 50 mg - 500 mg of α -tocopherol.

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58. (New) A method according to claim 57, wherein the raising is within 4 weeks.
59. (New) A method according to claim 57, wherein the method achieves a concentration of vitamin C in the blood plasma that is at least 80 $\mu\text{mol/liter}$.
60. (New) A method according to claim 57, wherein the method achieves, in blood plasma, a concentration of vitamin C of from about 102 to 142 $\mu\text{mol/liter}$, and a concentration of vitamin E of from about 46 to 65 $\mu\text{mol/liter}$.
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61. (New) A method according to claim 57, wherein the administration is of an at least once daily dose of dosage units comprising a slow release formulation only of vitamin C and a plain release formulation only of vitamin E.
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62. (New) A method according to claim 61, wherein the daily dose of vitamin E corresponds to 100 mg - 250 mg of α -tocopherol.
63. (New) A method according to claim 61, wherein the daily dose of vitamin C corresponds to 300 mg -600 mg of ascorbic acid.
64. (New) A method according to claim 61, wherein the at least once daily dose is delivered by at most 8 dosage units.

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65. (New) A method according to claim 61, wherein the at least once daily dose is delivered in 1 or 2 dosage units.

66. (New) A method according to claim 65, wherein the daily dose of vitamins C and E is delivered by 2 dosage units, each dosage unit comprising i) from approximately 200 to 300 mg of vitamin C and ii) approximately 80 to 120 mg of vitamin E.

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Sub B

67. (New) A method of treating oxidative stress disorders and associated diseases and conditions, said method comprising administering to an individual at least one dosage unit per day of a combination of vitamin C and vitamin E in sufficient amounts to raise the concentration of said vitamins in blood plasma sufficiently to treat at least one oxidative stress disorder and to a controlled ratio;

wherein said vitamin C is formulated only in a slow-release preparation and vitamin E is formulated only in plain-release formulation;

wherein the method achieves a concentration of vitamin E in the blood plasma of at least 20 $\mu\text{mol/liter}$, and a concentration of vitamin C in the blood plasma of at least 40 $\mu\text{mol/liter}$;

wherein the at least one dosage units delivers a daily dose corresponding to 60 mg - 2 g of vitamin C and a daily dose corresponding to 50 mg - 500 mg of α -tocopherol; and

wherein the formulation of vitamin E is such that at least 90% of vitamin E is dissolved in less than 30 minutes under the conditions of Test B, and the formulation of vitamin C is such that less than 40% of vitamin C is dissolved after 1 hour under the conditions of Test A.

Omnibus

68. (New) A method according to claim 67, wherein the controlled ratio is from 1:1 to 3:1 of vitamin C to vitamin E, as measured ~~within~~ 8 weeks from the first administration.

69. (New) A method according to claim 67, wherein the method achieves, in blood plasma, a concentration of vitamins C of from about 102 to 142 $\mu\text{mol/liter}$, and a concentration of vitamin E of from about 46 to 65 $\mu\text{mol/liter}$.

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70. (New) A method according to claim 67, wherein the at least one dosage unit is at most 8 dosage units.

71. (New) A method according to claim 70, wherein the at least one dosage unit is 1 or 2 dosage units.

72. (New) A method according to claim 67, wherein the daily administration is of a daily dose of vitamin E corresponding to 100 mg - 250 mg of α -tocopherol.

73. (New) A method according to claim 67, wherein the daily administration is of a daily dose of vitamin C corresponding to 250 mg - 750 mg of ascorbic acid.--

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